

## **RESPONSE**

### **I. Status of the Claims**

Prior to the fourth Action, claims 1-68 and 102-132 were pending and have been examined. Claims 14-18, 48, 54-65 and 118-130 have been allowed and claim 13 is only objected to. Claims 106, 107 and 108 should have been allowed as indirectly dependent on allowed claim 48.

Presently, claims 1-13, 19-47, 49-53, 66-68, 102-105, 109-117, 131 and 132 have been canceled without prejudice. No claims have been amended or added. Claims 14-18, 48, 54-65, 106-108 and 118-130 are therefore in the case. According to 37 C.F.R. § 1.121(c), a copy of the pending claims is provided in the amendment section.

### **II. Entry of Amendments**

The present amendments are entitled to entry after final rejection as the amendments cancel claims and expressly adopt the examiner's indications for allowance in the final Action. The amendments are therefore entitled to entry under 37 C.F.R. § 1.116.

### **III. Rejection of Claims 1-12, 19-47, 49-53, 66-68 and 102-117 Under 35 U.S.C. § 103(a)**

Claims 1-12, 19-47, 49-53, 66-68, 102-117, 131 and 132 are rejected under 35 U.S.C. § 103(a) as allegedly being legally obvious over Mikos *et al.*, U.S. Patent No. 5,514,378 ("Mikos"), Grinstaff *et al.*, U.S. Patent No. 5,639,473 ("Grinstaff") and Mineau-Hanschke, U.S. Patent No. 5,965,125 ("Mineau-Hanschke") in combination. Although Applicants respectfully traverse, the rejection is moot.

Applicants respectfully traverse the rejection for reasons of record, as summarized below. Nonetheless, Applicants note that claims 14-18, 48, 54-65 and 118-130 are allowed (fifth Action at summary page). Without acquiescing with the present rejections in any way, and particularly in light of patent term issues, Applicants presently elect to progress the allowed claims to issue.

Claims 106, 107 and 108 stand rejected over Mikos, Grinstaff and Mineau-Hanschke. The rejection of these claims is *prima facie* improper. In Applicants' last response, claims 106 and 108 were amended to indirectly depend from allowed claim 48, which was also highlighted in the remarks section. Claims 106, 107 and 108 are thus also in condition for allowance.

The rejection of the remaining claims over Mikos, Grinstaff and Mineau-Hanschke is also improper. Applicants respectfully incorporate by reference their earlier responses to this rejection, including that the references have been improperly combined, and that Mikos, Grinstaff and Mineau-Hanschke, even in combination, do not teach or suggest the presently claimed invention.

Importantly, the record shows that Mikos teaches away from the claimed invention's incorporation of nucleic acids into structural matrices as Mikos requires organic solvents and high temperatures. This was detailed in Applicants' last response.

In reply, the fifth Action first states "subjecting nucleic acid sequences not to high temperature or organic solvents is a simple modification of the method as taught by Mikos" (fifth Action at middle of page 5). This is not correct. Subjecting nucleic acid sequences to organic solvents is absolutely required by Mikos and there are no simple modifications of the Mikos methods that lead to the presently claimed invention.

The fifth Action next states that Mikos teaches "that the biocompatible porous polymer membranes are prepared by dissolving salt particles out of the membrane by immersing the membrane in water or another solvent in a water bath that is maintained at 37°C" and refers to Mikos at column 3, lines 19-22 and column 6, lines 41-64 (fifth Action at page 5, emphasis as in original). Dissolving salt particles out of membranes using water, preferably at 37°C, represents only the latter part of the Mikos methods.

The Mikos methods as a whole clearly require organic solvents to dissolve the polymer (not the salt) (see Mikos throughout) and Mikos states that the polymer is dissolved "most preferably [in] a volatile organic solvent" (Mikos column 5, lines 60-62). The Mikos methods as a whole also preferably use high temperatures (see Mikos throughout), such as 195°C, said to be approximately 15°C higher than the melting temperature of a PLLA polymer (see Mikos throughout, *e.g.*, column 6, lines 19-28, and column 8, lines 37-45).

Thus, Mikos absolutely requires organic solvents, which is inconsistent with the incorporation of nucleic acids, and no simple modifications of Mikos teach or suggest the presently claimed invention. In contrast to the Action at page 5, there is nothing Grinstaff and/or Mineau-Hanschke that could have "easily corrected" the failure of Mikos to teach or suggest the incorporation of nucleic acids into the Mikos materials, as there is nothing in Grinstaff and/or Mineau-Hanschke to correct the important deficiencies in the Mikos methods.

In any event, Grinstaff and Mineau-Hanschke have been improperly combined with Mikos and, even if combined, Mikos, Grinstaff and Mineau-Hanschke in combination fail to teach or suggest the structural matrix-nucleic acid compositions of the claimed invention.

Furthermore, Grinstaff and Mineau-Hanschke also teach away from the presently claimed invention. For example, Grinstaff concerns polymeric shells "for parenteral administration in aqueous suspension" (Grinstaff at column 6, lines 8-16), *i.e.*, *passive release*. This is the opposite of the active processes made possible by the "structural matrix" nucleic acid compositions of the claimed invention, *into which cells migrate, encounter and take up the nucleic acids and express the encoded products* (specification at pages 7, 8, 15, 25, 26, 38, 41, 56, 69, 76, 77, 78, 79, 81, 82 and 114).

Mineau-Hanschke is limited to collagen-microcapsule matrices that do not contain nucleic acid segments other than in the context of genetically engineered cells. Thus, Mineau-Hanschke teaches away from the claimed invention as it teaches that cells must be transfected with nucleic acids before contact with a matrix. The methods of Mineau-Hanschke suffer from important drawbacks, *e.g.*, the need to isolate and expand cells *in vitro* and by poor survival of many cell types following transplantation (see, *e.g.*, specification at page 29, lines 12-13). The matrix-nucleic acid compositions of the present invention, in contrast, provide a structural matrix *into which cells migrate, encounter, take up and express the nucleic acids located therein* and thus have important advantages for *in vivo* use.

Therefore, Mikos, Grinstaff and Mineau-Hanschke, either alone or in combination, do not teach or suggest the claimed invention. The § 103(a) rejection is therefore improper and should have been withdrawn. Although the § 103(a) rejection is improper, this issue is moot as it pertains to the present application.

#### **IV. Rejection of Claim 131 Under 35 U.S.C. § 103(a)**

Claim 131 is newly rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite in the phrase "substantially free from residues of organic solvents". Although Applicants respectfully traverse, the rejection is moot.

The proper test of definiteness is whether, in the light of the teachings of the prior art and of the particular application disclosure, the claims set out and circumscribe, for one possessing an ordinary level of skill in the pertinent art, a particular area with a reasonable degree of particularity. *In re Moore*, 169 USPQ 236 (C.C.P.A. 1971). The present use of the phrase "substantially free" clearly meets this test, particularly as the application disclosure distinguishes the invention from the prior art on this basis, as well as other grounds.

As to "substantially", the Federal Circuit has repeatedly approved of the use of "substantially" in claims. Expressions like 'substantially' are used to accommodate minor variations appropriate to secure an invention. The term 'substantially' is not indefinite when it serves reasonably to describe the scope of the subject matter and to distinguish it from the prior art. *Verve LLC vs. Crane Cams Inc.*, 65 USPQ2d 1051 (Fed. Cir. 2002). In particular, in *Verve LLC vs. Crane Cams Inc.*, the Federal Circuit summarized:

"Expressions such as 'substantially' are used in patent documents when warranted by the nature of the invention, in order to accommodate the minor variations that may be appropriate to secure the invention. Such usage may well satisfy the charge to 'particularly point out and distinctly claim' the invention, 35 U.S.C. §112, and indeed may be necessary in order to provide the inventor with the benefit of his invention. In *Andrew Corp. v. Gabriel Elecs. Inc.*, 847 F.2d 819, 821-22, 6 USPQ2d 2010, 2013 (Fed. Cir. 1988) the court explained that usages such as 'substantially equal' and 'closely approximate' may serve to describe the invention with precision appropriate to the technology and without intruding on the prior art. The court again explained in *Ecolab Inc. v. Envirochem, Inc.*, 264 F.3d 1358, 1367, 60 USPQ2d 1173, 1179 (Fed. Cir. 2001) that 'like the term 'about,' the term 'substantially' is a descriptive term commonly used in patent claims to 'avoid a strict numerical boundary to the specified parameter,' quoting *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217, 36 USPQ2d 1225, 1229 (Fed. Cir. 1995).

It is thus well established that when the term 'substantially' serves reasonably to describe the subject matter so that its scope would be understood by persons in the field of the invention, and to distinguish the claimed subject matter from the prior art, it is not indefinite. *Verve LLC vs. Crane Cams Inc.*, *supra*. Use of 'substantially' in the present case fulfills these roles and claim 131 is therefore sufficiently definite.

Although the § 112, second paragraph rejection is improper for the foregoing reasons, this issue is moot as it pertains to the present application.

## **V. Conclusion**

This is a complete response to the referenced Official Action. In conclusion, Applicants submit that the present case is in condition for allowance and such favorable action is

respectfully requested. Should Examiner Kaushal have any questions or comments, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,  
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